REMARKS

Applicants respectfully request reconsideration of the pending claims in view of the Amendment above and the remarks below.

1. STATUS OF THE CLAIMS

Claims 1-35 were originally filed in the present application. Claims 1-13 and 21-22 were elected in a Response mailed 9/27/2002 to a Restriction Requirement mailed 8/28/2002. Claims 14-20 and 23-35 were previously canceled or withdrawn. Claims 1-2, 4-5, 9-11, and 13 are canceled herein. Claims 3, 6-8 and 12 are amended herein. Claims 3, 6-8, 12, and 21-22 are currently pending.

Applicants canceled claims 1-2, 4-5, 9-11, and 13, but do not acquiesce to any grounds for their prior rejection. Applicants reserve their right to pursue the canceled subject matter in further prosecution.

2. DRAWINGS

Pursuant to the Office Action mailed December 13, 2002, submitted herewith are the formal drawings consisting of 4 sheets (Figures 1-7) of formal drawings for the above-identified application. Entry is respectfully requested.

3. REJECTION OF CLAIMS 5-8 AND 21-22 UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

Claims 5-8 and 21-22 were rejected under 35 U.S.C. § 112, first paragraph because the specification allegedly does not reasonably provide enablement. The present rejection is respectfully traversed. The following remarks are directed to claims 6-8 and 21-22 as claim 5 is canceled herein rendering the rejection of claim 5 moot.

a. Claim 6: Enablement

The Examiner alleges that claim 6 is not enabled because the specification "does not reasonably provide enablement for any monoclonal antibody that inhibits LBP-mediated binding of LPS to CD14". The Applicants respectfully traverse the present enablement rejection of claim 6.

The test for enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures coupled with information known in the art without undue experimentation.

The specification discloses and asserts enablement of the monoclonal antibody of claim 6. See, e.g., page 12, lines 28-32 and page 13, lines 2-5). The specification teaches that monoclonal antibodies immunoreactive with LBP can inhibit LPS binding to CD14 (see, e.g., page 4, lines 18-21) which was not known prior to the present disclosure. The specification discloses that monoclonals which immunoreact with LBP can be made through isolation from mammalian species (see, e.g., page 14, lines 7-9) or by other methods such as using hybridoma techniques (see, e.g., page 16, lines 28-29 and Example 1 at page 42). The specification discloses screening monoclonals that immunoreact with LBP to identify those that do not substantially inhibit LBP binding to LPS (see, e.g., page 42, lines 23-24 and pages 55-58). The specification discloses screening the monoclonals to identify those antibodies that inhibit LBP-mediated binding of LPS to CD14 (see, e.g., Example 2C particularly page 50, line 9 through page 52, line 25). The specification further discloses methods for screening monoclonal antibodies to identify those having the immunospecificity of antibodies of the present invention (see, e.g., page 15, line 16 through page 16, line 11). Examples of the use of the claimed antibodies is disclosed, for instance, at page 19, line 31 through page 41, line 19.

Thus, the specification discloses how to produce and screen for the claimed antibodies. Practitioners of art are prepared to produce and screen numerous antibodies in order to identify the desired antibodies. One experiment is not simply the screening of one antibody or hybridoma but rather is the entire attempt to make the desired antibody. See, e.g, In re Wands 858 F.2d at 737, 8 USPQ2d at 1400 (Fed. Cir. 1988).

In view of the specification and the knowledge in the art, one skilled in the art can produce monoclonal antibodies having each of the limitations recited in claim 6, without undue experimentation.

Next, the Examiner argues that claim 6 is drawn to a monoclonal antibody that inhibits LBP-mediated binding of LPS to CD14. The Examiner alleges, however, that only monoclonal antibodies 1E8, 2B5, and 18G4 inhibited binding of LPS by CD14-expressing CHO cells in Example 2C.

It is irrelevant that all antibodies recited in claim 6, as amended, allegedly are not discussed in Example 2C. The Examiner must look to the specification as a whole to determine whether or not a claim is enabled. As discussed immediately above, the Applicants point out, using references to specific disclosures in the specification, that one skilled in the art is able to make and use the monoclonal antibody of claim 6 without undue experimentation.

b. Claims 7 and 8: Enablement

The Examiner alleges that the specification appears to fail to recite specifically which antibodies meet the limitations recited in claims 7 and 8. The present rejection is respectfully traversed.

Claims 7 and 8 each depend from claim 6 and, therefore, include all limitations of claim 6. The enablement of the limiting elements of claim 6 are discussed above. Claim 7, further to claim

6, recites the limitation that the claimed monoclonal antibody inhibits LBP-mediated LPS-dependent activation of myeloid cells. Claim 8, further to claim 6, recites the limitation that the claimed monoclonal antibody inhibits LBP-mediated LPS-dependent secretion of tumor necrosis factor (TNF) from myeloid cells.

The specification discloses which antibodies meet the limitations recited in claims 7 or 8, for example, at page 13, lines 2-5 and in the claims as originally filed. The specification discloses making the claimed antibodies, for instance, in Example 1 at page 42. Example 2C at page 50 discloses a method of screening monoclonal antibodies made in Example 1 for inhibition of LBP-mediated LPS-dependent activation of myeloid cells and inhibition of LBP-mediated LPS-dependent secretion of tumor necrosis factor from myeloid cells. The specification discloses how to use the claimed antibodies, for example, at page 19, line 31 through page 41, line 19.

In view of the present disclosure and knowledge in the art, one skilled in the art is able to screen monoclonal antibodies to identify those that inhibit the activation of myeloid cells (claim 7) or the TNF secretion from myeloid cells (claim 8). Accordingly, one skilled in the art is able to make and use the claimed antibodies in view of the specification and knowledge available in the art, without undue experimentation.

The Examiner further alleges that the "Applicant is broadly claiming a monoclonal antibody having the recited properties, but has only provided evidence of a single example".

Under the enablement provisions of the patent statutes, the Applicant is not required to provide any "working examples" but rather is required to describe how to make and use the invention in such detail to one skilled in the art as to enable the invention. The fact that the specification is devoid of a working example, includes one, or includes multiple working examples is without significance. It is well established that examples are not

necessary. *Ex parte Nardi and Simier*, 229 USPQ 79, 80 (BOPA, 1986).

The Examiner next alleges that "Applicants other monoclonal antibodies do not have the recited properties".

The Examiner does not indicate which "other" monoclonal antibodies allegedly do not have the recited properties. The Applicant is only required to enable one skilled in the art to make and use the invention as claimed. The specification provides enabling disclosures for the monoclonal antibodies of claims 7 and 8 as discussed above.

Next the Examiner alleges that "one of skill in the art would be required to perform undue experimentation to find monoclonal antibodies that have the recited properties when the specification clearly teaches that only a few antibodies have the recited properties".

Practitioners of art are prepared to produce and screen numerous antibodies in order to identify the desired antibodies. One experiment is not simply the screening of one antibody or hybridoma but rather is the entire attempt to make the desired antibody. See, e.g, In re Wands 858 F.2d at 737, 8 USPQ2d at 1400 (Fed. Cir. 1988).

The specification discloses how to produce and screen for the claimed monoclonal antibody. For example, the specification discloses an assay of TNF release from whole human blood (see, e.g., page 58, line 25 through page 60, line 17). TNF release is disclosed to be released from myeloid cells which is also an indicator of the activation of myeloid cells (see, e.g., page 13, lines 8-19). Thus, the present assay provides a screening method to identify antibodies that inhibit LBP-mediated LPS-dependent activation of myeloid cells (recited in claim 7) and TNF secretion from myeloid cells (recited in claim 8). Accordingly, the invention is described in sufficient detail to enable one skilled in the art can make and use the claimed invention without undue

experimentation.

c. Claims 21 and 22: Enablement

The Examiner alleges that claims 21 and 22 are not enabled. See the first line of item #5 on page 3 of the Office Action. The present rejection is respectfully traversed.

Claim 21 depends from claim 7. Discussion regarding the enablement of claim 7 is provided above. Claim 21 is directed to a pharmaceutical composition comprising the monoclonal antibody of claim 7 in a pharmacological carrier. Claim 22 depends from claim 21 and is directed to a pharmaceutical composition comprising two or more monoclonal antibodies of claim 7 in a pharmacological carrier. The specification discloses how to make and use the pharmaceutical compositions of claims 21 and 22, for example, at page 20, line 11 through page 23, line 20; at page 23, line 22 through page 30, line 25; and at page 19, line 31 through page 41, line 19.

In view of the disclosures in the specification and the knowledge in the art, at the time the application was filed, one skilled in the art is able to make and use the present invention without undue experimentation. The Applicants respectfully request that the present rejection be withdrawn.

4. REJECTION OF CLAIMS 1-13 AND 21-22 UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

Claims 1-13 and 21-22 were rejected under 35 U.S.C. § 112, first paragraph as containing subject matter that allegedly was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the applicant was filed, had possession of the claimed invention. The present rejection is respectfully traversed. Claims 1-2, 4-5, 9-11, and 13 are canceled herein; therefore, the present rejection of claims 1-2, 4-5, 9-11, and 13 is moot. The following

discussion is directed to currently pending claims 3, 6-8, 12, and 21-22.

Referring to claims 3, 6-8, and 12, the specification discloses the binding specificity of each of Mab 4D7, Mab 5C5, Mab 6B6, Mab 8C9, Mab 18G4, or Mab 24B7 to LBP, to denatured LBP and to the complex of LBP:LPS at page 53, line 12 through page 55, line 2 and Figure 4. In view of the specification including Figure 4, one skilled in the art can determine the binding specificity of each Mab (claims 3 and 6-8) or Mab produced by a hybridoma cell line (claim 12) for each respective form of LBP. One skilled in the art can, thus, determine if a given monoclonal antibody is encompassed by the claims. Therefore, one skilled in the art does not need to obtain Mab 4D7, Mab 5C5, Mab 6B6, Mab 8C9, Mab 18G4, or Mab 24B7 from a deposit to practice the claimed invention. Mab 4D7, Mab 5C5, Mab 6B6, Mab 8C9, Mab 18G4, and Mab 24B7 are described in the specification, for example, at page 42, lines 28-29. The claimed invention can be practiced in view of the disclosure set forth in the specification.

Furthermore, the specification describes the production of hybridoma cell lines that produce monoclonal antibodies which immunoreact with LBP, for example, at page 42, lines 2-15. A description of a screening process to identify monoclonals that do not substantially inhibit LBP binding to LPS is disclosed, for example, at page 55, line 4 through page 56, line 3. A description of screening monoclonal antibodies to identify those that inhibit LBP-mediated binding to LPS to CD14 is disclosed, for example, at page 50, line 9 through page 52, line 25. The binding specificity of Mab 4D7, Mab 5C5, Mab 6B6, Mab 8C9, Mab 18G4, or Mab 24B7 to LBP, denatured LBP, and a complex including LBP and LPS are described in the specification, for example, at page 53, line 12 through page 55, line 2 and Figure 4. A description of how to use the claimed monoclonal antibody is disclosed in the specification, for example, at page 19, line 31 through page 41, line 19.

Each monoclonal antibody is produced by a specific hybridoma cell line. Accordingly, the above screening processes reproducibly lead to the identification of the claimed monoclonal antibodies and to the hybridoma cell lines that produce each monoclonal. Therefore, the specification describes the subject matter in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 21 and 22 are dependent on claim 7. Discussion regarding the description of the subject matter of claim 7, as provided in the specification, is set forth immediately above and is applicable to claims 21 and 22. Claim 21 is directed to a pharmaceutical composition comprising the monoclonal antibody of claim 7 in a pharmacological carrier. The specification describes how to reproducibly make the claimed pharmaceutical composition, for example, at page 20, line 11 through page 23, line 20 and at page 23, line 22 through page 30, line 25. The specification describes how to use the claimed pharmaceutical composition, for example, at page 19, line 31 through page 41, line 19.

Claim 22 is directed to the pharmaceutical composition of claim 21 wherein the composition contains two or more different monoclonal antibodies. The inclusion of two or more different monoclonal antibodies into a pharmaceutical composition is well known in the art and is described in the specification, for example, at page 20, lines 15-19 and page 69, lines 13-15.

The Applicants respectfully submit that the above identified teachings in the specification regarding claims 21 and 22 constitute a written description so as to reasonably convey to one skilled in the art that the Applicants had possession of the claimed invention at the time the application was filed.

Thus, it is submitted that each claim is described in the specification sufficiently to demonstrate to one skilled in the art that the inventors were in possession of the invention at the

time the application was filed. The Applicants respectfully request that the present rejection be withdrawn.

5. REJECTION OF CLAIMS 3, 6, AND 12 UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

Claims 3, 6, and 12 were rejected under 35 U.S.C. § 112, second paragraph, as being allegedly indefinite. The present rejection is respectfully traversed. However, the claim amendments submitted herein render the present rejection moot. The Applicants respectfully request that the present rejection be withdrawn.

6. REJECTION OF CLAIMS 1-13 and 21-22 BASED ON OBVIOUSNESS-TYPE DOUBLE PATENTING

Claims 1-13 and 21-22 were rejected based on obviousness-type double patenting over claims 1-5 and 8-15 of U.S. Patent No. 5,753,504. The present rejection is respectfully traversed. Claims 1-2, 4-5, 9-11, and 13 are canceled herein; therefore, the present rejection of claims 1-2, 4-5, 9-11, and 13 is moot. The following discussion is directed to currently pending claims 3, 6-8, 12, and 21-22.

Claim 3, as amended, recites an element of the claimed monoclonal antibody including a binding specificity to LBP, to denatured LBP, and to a complex containing LBP and LPS of Mab 4D7, Mab 5C5, Mab 6B6, Mab 8C9, Mab 18G4, or Mab 24B7. Claims 1-5 and 8-15 of U.S. Patent 5,753,504 do not recite that claimed element. Therefore, obviousness-type double patenting over claims 1-5 and 8-15 of U.S. Patent 5,753,504 cannot exist.

Claims 6-8, as amended, recite an element of the claimed monoclonal antibody including a binding specificity to LBP, to denatured LBP, and to a complex containing LBP and LPS of Mab 4D7, Mab 5C5, Mab 6B6, Mab 18G4, or Mab 24B7. Claims 1-5 and 8-15 of U.S. Patent 5,753,504 do not recite that claimed element. Therefore, obviousness-type double patenting over claims 1-5 and

8-15 of U.S. Patent 5,753,504 cannot exist.

Claim 12, as amended, recites an element of a hybridoma cell line that produces a monoclonal antibody including a binding specificity to LBP, to denatured LBP, and to a complex containing LBP and LPS of Mab 4D7, Mab 5C5, Mab 6B6, Mab 18G4, or Mab 24B7. Claims 1-5 and 8-15 of U.S. Patent 5,753,504 do not recite that claimed element. Therefore, obviousness-type double patenting over claims 1-5 and 8-15 of U.S. Patent 5,753,504 cannot exist.

Claims 21-22 recite a pharmaceutical composition comprising the monoclonal antibody of claim 7 in a pharmaceutical carrier. Claim 21 depends from claim 7 which depends from claim 6 and, thus, includes the limitation that the recited monoclonal antibody includes a binding specificity to LBP, to denatured LBP, and to a complex containing LBP and LPS of Mab 4D7, Mab 5C5, Mab 6B6, Mab 18G4, or Mab 24B7. Claims 1-5 and 8-15 of U.S. Patent 5,753,504 do not recite that claimed element. Therefore, obviousness-type double patenting over claims 1-5 and 8-15 of U.S. Patent 5,753,504 cannot exist.

The Applicants respectfully request that the present rejection be withdrawn.

7. REJECTION OF CLAIMS 1-8 and 11-13 UNDER 35 U.S.C. § 102(b)

a. Alleged Anticipation by Leturcq et al.

The Examiner alleges that claims 1-8 and 11-13 are anticipated under 35 U.S.C. § 102(b) by Leturcq et al. The present rejection is respectfully traversed. Claims 1-2, 4-5, 9-11, and 13 are canceled herein; therefore, the present rejection of claims 1-2, 4-5, 11, and 13 is moot. The following discussion is directed to the present rejection of pending claims 3, 6-8 and 12.

Claim 3, as amended, recites a monoclonal antibody including a binding specificity to LBP, to denatured LBP, and to a complex containing LBP and LPS of Mab 4D7, Mab 5C5, Mab 6B6, Mab 8C9, Mab

18G4, or Mab 24B7. Leturcq et al., does not teach that claimed element. Therefore, Leturcq et al., cannot anticipate claim 3.

Claims 6-8 recite, or depend from a claim that recites, a monoclonal antibody that inhibits LBP-mediated binding of LPS to CD14. Leturcq et al. does not teach a monoclonal antibody that inhibits LBP-mediated binding of LPS to CD14. Therefore, Leturcq et al., cannot anticipate claims 6-8.

Claim 12 recites a hybridoma cell line that produces a monoclonal antibody that inhibits LBP-mediated binding of LPS to CD14. Leturcq et al. does not teach a monoclonal antibody that inhibits LBP-mediated binding of LPS to CD14. Therefore, Leturcq et al., cannot anticipate claim 12.

The Applicants respectfully request that the present rejection be withdrawn.

b. Alleged Anticipation by Pugin et al.

The Examiner alleges that claims 1-8 and 11-13 are anticipated under 35 U.S.C. § 102(b) by Pugin et al. The present rejection is respectfully traversed.

The publication date for Pugin et al. was April 1993. The present application claims priority to U.S. Serial Number 08/153,364 filed on November 16, 1993. Pugin et al., was not published more than one year prior to the date of application for patent in the United States. Therefore, Pugin et al., is not an appropriate prior art citation against the present application. The Applicants respectfully request that the present rejection be withdrawn.

Attached hereto is Appendix I which is a marked-up version showing the changes made to the claims.

The Examiner is requested to contact the representative for the Applicants, to discuss any questions or for clarification. If

there are any further fees associated with this response, the Director is authorized to charge our Deposit Account No. 19-0962.

Respectfully submitted,

June 13, 2003
Date

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APPENDIX I
VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Claim 3 has been amended as follows:

3. (Once Amended) [The]A monoclonal antibody [of claim 1 wherein said antibody has a binding specificity for the epitope defined by Mab 1E8, Mab 2B5,]that immunoreacts with lipopolysaccharide (LPS) binding protein (LBP), but does not substantially inhibit LBP binding to LPS; the monoclonal antibody including a binding specificity to LBP, to denatured LBP, and to a complex containing LBP and LPS of Mab 4D7, Mab 5C5, Mab 6B6, Mab 8C9, [Mab 8F5,]Mab 18G4, or Mab 24B7.

Claim 6 has been amended as follows:

6. (Once Amended) [The]A monoclonal antibody [of claim 5 wherein said antibody has a binding specificity for the epitope defined by Mab 1E8, Mab2B5,]that immunoreacts with lipopolysaccharide (LPS) binding protein (LBP), inhibits LBP-mediated binding of LPS to CD14, but does not substantially inhibit LBP binding to LPS, the monoclonal antibody including a binding specificity to LBP, to denatured LBP, and to a complex containing LBP and LPS of Mab 4D7, Mab 5C5, Mab 6B6, Mab 18G4, or Mab 24B7.

Claim 7 has been amended as follows:

7. (Once Amended) The monoclonal antibody of claim [5]6, wherein [said]the monoclonal antibody inhibits LBP-mediated LPS-dependent activation of myeloid cells.

Claim 8 has been amended as follows:

8. (Once Amended) The monoclonal antibody of claim [5]6, wherein [said]the monoclonal antibody inhibits LBP-mediated LPS-dependent secretion of tumor necrosis factor from myeloid cells.

Claim 12 has been amended as follows:

12. (Once Amended) [The]A hybridoma cell line [of claim 11 wherein said antibody has a binding specificity for the epitope defined by Mab1E8, Mab 2B5,]that produces a monoclonal antibody that immunoreacts with lipopolysaccharide (LPS) binding protein (LBP), inhibits LBP-mediated binding of LPS to CD14, but does not substantially inhibit LBP binding to LPS, the monoclonal antibody including a binding specificity to LBP, to denatured LBP, and to a complex containing LBP and LPS of Mab 4D7, Mab 5C5, Mab 6B6, [Mab 8C9, Mab 8F5,]Mab 18G4, or Mab 24B7.